

**Remarks**

After entry of the amendment, claims 3-7 and 10-23 are pending.

Claims 1-7 have been editorially amended to change the term "1-benzyl-4-(5,6-dimethoxy-1-indanon)2-yl)methylpiperidine" to the equivalent term "donepezil."

Claim 5 has been amended to incorporate the subject matter of claim 9.

Claims 8 and 9 have been canceled without prejudice.

New claims 10-23 are supported by the specification at page 1, lines 6-8 and 26-30; page 3, lines 11-12; page 4, lines 20-22; page 5, lines 10-12; page 7, lines 26-31; and page 11 at Table 2.

No issues of new matter should arise and entry of the amendment is respectfully requested.

**Powers of Attorney**

Applicants are filing herewith an executed Power of Attorney signed by inventor Birol Emir on July 31, 2006, and an executed Power of Attorney signed by inventor Ponni Subbiah on July 31, 2006. The executed Powers of Attorney revoke the previous powers of attorney and grant power of attorney to the firm and address associated with Customer No. 26694.

**Information Disclosure Statement**

With respect to the Information Disclosure Statement filed June 28, 2004, Applicants respectfully bring the Examiner's attention to Table 1 in Rogers et al, *Arch Intern Med*, 158:1021-1031 (1998).

**First Rejection under 35 USC § 102**

Claims 5-8 are rejected under 35 USC § 102 over Shua-Haim et al, *Annals of Long-Term Care*, 7(2):67-71 (1999). Shua-Haim provides anecdotal reports for two patients allegedly having a Mini-Mental State Examination score of 0. Applicants respectfully submit that the amendment to claim 5 to include the subject matter of claim 9 (i.e., a Mini-Mental State Examination score of 5 to 9) overcomes the rejection. In view thereof, Applicants respectfully request that the rejection be withdrawn.

**Second Rejection under 35 USC § 102**

Claims 3-9 are rejected under 35 USC § 102 as being anticipated by Feldman et al, *Neurology*, 57:613-620 (August 2001).

Applicants respectfully traverse the rejection and respectfully submit that Feldman does not anticipate the claimed invention. At Table 1, Feldman discloses that the Mini-Mental State Examination score for the patients in the study was  $11.72 \pm 0.35$ , which is greater than the claimed score of 5 to 9. Moreover, Feldman does not disclose or suggest that severe Alzheimer's dementia is characterized by a Mini-Mental State Examination score of 5 to 9. In view thereof, Applicants respectfully request that the rejection be withdrawn.

**Rejections under 35 USC § 103 and Obviousness-Type Double Patenting**

(1) Claims 3-9 are rejected under 35 USC § 103 as being obvious over US Patent No. 5,100,901.

(2) Claims 3-9 are rejected under 35 USC § 103 as being obvious over US Patent No. 4,895,841.

(3) Claims 3-9 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 9 and 10 of US Patent No. 5,100,901.

(4) Claims 3-9 are rejected under the judicially created doctrine of obviousness-type double patenting over claims 12 and 13 of US Patent No. 4,895,841.

Applicants note that US Patent Nos. 5,100,901 and 4,895,841 have identical specifications because US Patent No. 5,100,901 is a divisional application of US Patent No. 4,895,841. Claims 9<sup>1</sup> and 10<sup>2</sup> in US Patent No. 5,100,901 recite the same limitations as claims 12<sup>3</sup> and 13<sup>4</sup> in US Patent No. 4,895,841. In view thereof, Applicants will address both patents and all four rejections at the same time.

Applicants respectfully traverse the rejections and respectfully submit that the '901 and '841 patents do not disclose, suggest, or provide a reasonable expectation of success for administering donepezil to patients with severe Alzheimer's dementia having a Mini-Mental State Examination score of 5 to 9.

As described in the specification of the pending application, the pathology of mild and moderate Alzheimer's dementia is completely different from the pathology of severe Alzheimer's

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<sup>1</sup> Claim 9 in the '901 patent recites "A method as claimed in claim 7, in which the disease is senile dementia."

<sup>2</sup> Claim 10 in the '901 patent recites "A method as claimed in claim 7, in which the disease is senile dementia of the Alzheimer type."

<sup>3</sup> Claim 12 in the '841 patent recites "A method as claimed in claim 11, in which the disease is the senile dementia."

<sup>4</sup> Claim 13 in the '841 patent recites "A method as claimed in claim 11, in which the disease is senile dementia of the Alzheimer type."

dementia.<sup>5</sup> Mild and moderate Alzheimer's dementia is characterized by a generalized atrophy of the brain, the appearance of senile plaques of the cerebral cortex, change to neurofibrils, abnormalities in cholinergic neurons, and a decrease in acetylcholine.<sup>6</sup> Severe Alzheimer's dementia is characterized by a loss of neural structure within the brain, a marked drop in brain volume, and a significant decrease in blood flow within the brain.<sup>7</sup> Moreover, the Alzheimer's Disease Assessment Scale, cognitive subscale (ADAS-cog) that is used to diagnosis and evaluate mild and moderate Alzheimer's dementia cannot be used to diagnosis and evaluate severe Alzheimer's dementia.<sup>8</sup>

The '901 and '841 patents discuss compounds, such as donepezil, that are acetylcholinesterase inhibitors. It was discovered that donepezil was useful for treating mild and moderate Alzheimer's dementia; however, it would not be expected that donepezil would be useful for treating severe Alzheimer's dementia because severe Alzheimer's dementia has a different pathology than mild/moderate Alzheimer's dementia. For example, it would not be expected that donepezil, which is useful for treating a disease characterized by abnormalities in cholinergic neurons and/or a decrease in acetylcholine (i.e., mild/moderate Alzheimer's dementia), would also be useful for treating a disease characterized by a loss of neural structure within the brain (i.e., severe Alzheimer's dementia). If there is a loss of neural structure, it would not be expected that an acetylcholinesterase inhibitor, i.e., donepezil, would be a successful treatment.

In view of the fact that the '901 and '581 patents disclose compounds having mechanisms of action that would be useful for treating mild/moderate Alzheimer's dementia and not severe Alzheimer's dementia (i.e., in view of the different pathologies of the diseases), one skilled in the art would not have a reasonable expectation that donepezil would be useful for treating severe Alzheimer's dementia.

In view thereof, the pending claims are unobvious over the specifications and claims of the '901 and '841 patents. Applicants respectfully request that the rejections be withdrawn.

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<sup>5</sup> Specification at page 2, lines 8-9.

<sup>6</sup> Specification at page 1, lines 16-22.

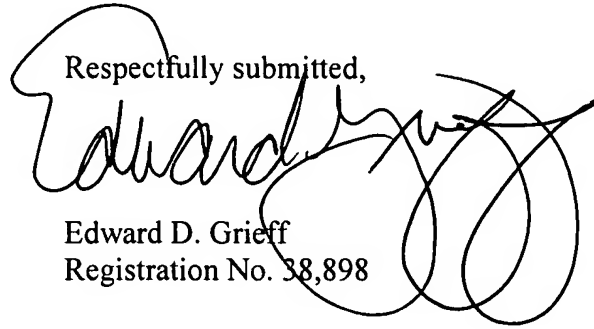
<sup>7</sup> Specification at page 2, lines 5-9.

<sup>8</sup> Specification at page 2, line 11 to page 3, line 2.

**Conclusion**

An early and favorable reconsideration and allowance of claims 3-7 and 10-23 is respectfully requested. The Examiner is encouraged to contact the undersigned to expedite prosecution of this application.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'Edward D. Grieff', is written over the typed name and registration number.

Edward D. Grieff  
Registration No. 38,898

Date: September 26, 2006

Venable LLP  
575 7th Street, NW  
Washington, DC 20004  
Phone: 202-344-4382